



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------------------|-------------|----------------------|---------------------|------------------|
| 10/578,385 | 05/11/2007 | Joseph J. Barchi | NIHA-0278 | 1844 |
| 45160 | 7590 | 11/23/2011 | EXAMINER | |
| OTT- NIH | | | DENT, ALANA HARRIS | |
| c/o WOODCOCK WASHBURN LLP | | | ART UNIT | PAPER NUMBER |
| CIRA CENTRE, 12TH FLOOR | | | | 1643 |
| 2929 ARCH STREET | | | | |
| PHILADELPHIA, PA 19104-2891 | | | | |
| NOTIFICATION DATE | | DELIVERY MODE | | |
| 11/23/2011 | | ELECTRONIC | | |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

eofficemonitor@woodcock.com

| | | | |
|------------------------------|--------------------------|---------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 10/578,385 | BARCHI ET AL. | |
| | Examiner | Art Unit | |
| | Alana Harris Dent, Ph.D. | 1643 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 19 September 2011.
- 2a) This action is **FINAL**. 2b) This action is non-final.
- 3) An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.
- 4) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 5) Claim(s) 43-47, 49-76 and 80-144 is/are pending in the application.
 - 5a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 6) Claim(s) _____ is/are allowed.
- 7) Claim(s) 43-47, 49-76 and 80-144 is/are rejected.
- 8) Claim(s) _____ is/are objected to.
- 9) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 10) The specification is objected to by the Examiner.
- 11) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 12) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ . |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ . | 6) <input type="checkbox"/> Other: _____ . |

DETAILED ACTION

Response to Amendment

1. Claims 43-47, 49-76 and 80-144 are pending.
Claims 1-13, 15-41 and 48 have been cancelled.
Claims 43, 47, 49-51 and 70 have been amended.
Claims 80-144 have been added.
Claims 43-47, 49-76 and 80-144 are examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objection

Claim Objections

3. The objection of claims 43 and 51 is withdrawn because both claims now cite GM₃ for continuity within the claims.

Withdrawn Rejections

Claim Rejections - 35 USC § 112

4. The rejection of claims 50 and 71 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in light of the amendment to the claims.

Claim Rejections - 35 USC § 103

5. The rejection of claims 43-47, 50-59, 63, 65-69 and 72-75 under 35 U.S.C. 103(a) as being unpatentable over Ragupathi et al. (Cancer Immunol. Immunother. 48: 1-8, 1999/ IDS reference number 11 submitted February 26, 2008), and further in view of Lloyd, K.O. (Drug News. Perspect. 13(8): 463-470, October 2000/ IDS reference 12 submitted February 26, 2006), WO document, WO 02/32404 A2 (published 25 April 2002), and Otsuka et al. (J. Am. Chem. Soc. 123: 8226-8230, 2001/ IDS reference 7 submitted February 26, 2008) is withdrawn in light of amendments to independent claim 43.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 70-76, 106-112 and 140-144 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 70-76, 106-112 and 140-144 contain the phrase "...at least a portion of the antigen-nanoparticle conjugates..." or "...at least a portion of the nanoparticles...". It is not clear from the claims what part or section of the antigen nanoparticle reads on a portion. For example, it is not clear if it is half, a third or just the antigen part of the conjugate. Accordingly, the meters and bounds of the claims cannot be determined and Applicants are requested to clarify.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. Claims 43-47, 49-76 and 80-144 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ragupathi et al. (Cancer Immunol. Immunother. 48: 1-8, 1999/ IDS reference number 11 submitted February 26, 2008), and further in view of Lloyd, K.O. (Drug News. Perspect. 13(8): 463-470, October 2000/ IDS reference 12 submitted February 26, 2006), WO document, WO 02/32404 A2 (published 25 April 2002), Otsuka et al. (J. Am. Chem. Soc. 123: 8226-8230, 2001/ IDS reference 7 submitted February 26, 2008) and Ashdown/ US Patent Application Publication No.: US 2005/0180971 A1 (effective filing date February 14, 2003). Ragupathi teaches the administration of vaccines comprising sialyl-Tn or clustered STn [STn(c)]-keyhole limpet hemocyanin (KLH) conjugates linked with 4-(4-maleimidomethyl)cyclohexane-1-carboxyl hydrazide (MMCCH) linkers to mice and LS-C human colon cancer cells, see Abstract on page 1; and page 2, "Vaccine..." and "Animals..." sections. Ragupathi does not teach the said plurality of Tn antigens (expressed on colon and prostate tumors) with additional carbohydrate antigens, such as fucosyl GM1 antigen, T-F and Lewis Y antigen in

a nanoparticle administered to a human. Ragupathi also does not teach the removal of tumor cells from the mammal before the antigen-nanoparticle conjugate is administered.

However, Lloyd teaches different carbohydrate antigens, GM1 (expressed on small-cell lung cancer), Lewis Y (expressed on tumors of lung and prostate), T-F (expressed on tumors of breast and prostate) can be administered to subjects in vaccine formulations, see the entire reference. Lloyd also teaches epitopes can exist on the cell surface, see page 464, 2nd column. The WO document teaches nanoparticles comprising carbohydrate groups and implementation in therapy and medical treatment including inhibiting metastasis of cancer, see abstract; page 4, lines 4-14; page 12, lines 14-23; and page 14, lines 15-28. The nanoparticles of the antigen-nanoparticles conjugates have one or more carbohydrate groups, the mean diameter between 0.5 and 100nm, 100 to 500 gold atoms, see page 4, line 31-page 5, line 17; and page 7, lines 1-25. Otsuka teaches PEGylated gold nanoparticles comprising a gold-thiol linkage produced after chemical reduction with NaBH₄. Lastly, Ashdown teaches methods for treating cancer including breast cancer with the removal of all tumor cells, as well as administering a tumor antigen vaccine, see abstract; page 2, section 0026; page 3, section 0041; and page 4, section 0065. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the teachings of all references to

Art Unit: 1643

combine a plurality of target carbohydrate cancer antigens as an immunogenic polyvalent antitumor vaccine, see all documents in their entirety. It would have been *prima facie* obvious to one ordinary skill in the art at the time of the claimed invention to remove the tumor cells to reduce the patient's tumor load in hopes of increasing the anti-tumor response, see page 3 of Ashdown, sections 0047 and 0048. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings in all the references, an antigen-nanoparticle formulation would be effective in producing antibodies that are capable of reacting with tumor cells, consequently reducing/eliminating the tumor and ultimately destroying tumors that express these antigens.

10. Claims 80-84, 87-117 and 120-144 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ragupathi et al. (Cancer Immunol. Immunother. 48: 1-8, 1999/ IDS reference number 11 submitted February 26, 2008), and further in view of Lloyd, K.O. (Drug News. Perspect. 13(8): 463-470, October 2000/ IDS reference 12 submitted February 26, 2006), WO document, WO 02/32404 A2 (published 25 April 2002) and Otsuka et al. (J. Am. Chem. Soc. 123: 8226-8230, 2001/ IDS reference 7 submitted February 26, 2008). Ragupathi teaches the administration of vaccines comprising sialyl-Tn or clustered STn [STn(c)]-keyhole limpet hemocyanin (KLH) conjugates linked with 4-(4-

Art Unit: 1643

maleimidomethyl)cyclohexane-1-carboxyl hydrazide (MMCCH) linkers to mice and LS-C human colon cancer cells, see Abstract on page 1; and page 2, “Vaccine...” and “Animals...” sections. Ragupathi does not teach the said plurality of Tn antigens (expressed on colon and prostate tumors) with additional carbohydrate antigens, such as fucosyl GM1 antigen, T-F and Lewis Y antigen in a nanoparticle administered to a human.

However, Lloyd teaches different carbohydrate antigens, GM1 (expressed on small-cell lung cancer), Lewis Y (expressed on tumors of lung and prostate), T-F (expressed on tumors of breast and prostate) can be administered to subjects in vaccine formulations, see the entire reference. Lloyd also teaches epitopes can exist on the cell surface, see page 464, 2nd column. The WO document teaches nanoparticles comprising carbohydrate groups and implementation in therapy and medical treatment including inhibiting metastasis of cancer, see abstract; page 4, lines 4-14; page 12, lines 14-23; and page 14, lines 15-28. The nanoparticles of the antigen-nanoparticles conjugates have one or more carbohydrate groups, the mean diameter between 0.5 and 100nm, 100 to 500 gold atoms, see page 4, line 31-page 5, line 17; and page 7, lines 1-25. Otsuka teaches PEGylated gold nanoparticles comprising a gold-thiol linkage produced after chemical reduction with NaBH₄. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the teachings of all references to combine a plurality of

Art Unit: 1643

target carbohydrate cancer antigens as an immunogenic polyvalent antitumor vaccine, see all documents in their entirety. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings in all the references, an antigen-nanoparticle formulation would be effective in producing antibodies that are capable of reacting with tumor cells, consequently reducing/eliminating the tumor and ultimately destroying tumors that express these antigens.

Conclusion

11. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571)272-0831. The Examiner works a **flexible schedule**, however she can generally be reached Monday through Friday, 8 am to 6 pm.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Misook Yu, Ph.D. can be reached on (571)272-0839. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Alana M. Harris Dent, Ph.D.
15 November 2011
/Alana Harris Dent, Ph.D./
Primary Examiner, Art Unit 1643